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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/825,757	LINNEN ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *116,125-131 and 140-144* is/are pending in the application.

4a) Of the above claim(s) *131 and 140-144* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *116 and 125-130* is/are rejected.

7)☒ Claim(s) *116, 125-130* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/31/2005, 10/08/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/08/2009 has been entered.

2. Claims 116, 125-131, 140-144 are pending. Claims 1-115, 117-124, 132-139, 145-183 are cancelled.

3. Claims 131 and 140-144 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/26/2006.

4. The following rejections for Claims 116 and 125-130 are set forth below. It is noted that these rejections are newly applied based upon amendments to the claims and further consideration.

5. This action is NONFINAL.

Withdrawn Rejections

6. The rejection of the claims under 35 USC 102(e) made in section 9 of the previous office action (1/08/2009) has been withdrawn based upon amendments to the claims.

7. The rejection of the claims under 35 USC 103(a) made in section 11 of the previous office action (1/08/2009) has been withdrawn after further consideration of the amendments to the claims and arguments made in the reply.

Request to Correct Inventorship

8. In view of the papers filed 10/26/2006, the inventorship in this nonprovisional application has been changed by the deletion of Jeffrey M. Linnen and Daniel L. Kacian.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Priority

9. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/469294 filed 5/09/2003, Application No. 60/465428 filed 4/25/2003, and Application No. 60/464049 filed 4/17/2003, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Specifically, all three applications fail to disclose SEQ ID No. 4 and 7, therefore there does not appear to be support for the applicant's presently claimed invention in these provisional applications. Applications 60/469294 and 60/465428 both provide 15 SEQ ID Numbers and 25 SEQ ID Numbers respectively. However, none of these sequences appear to be identical to SEQ ID No. 4 or 7 nor do these sequences encompass SEQ ID No. 4 or 7. Application 60/464049 does not provide any sequences and therefore does not support the recitation of SEQ ID No. 4 and 7. As a result the earliest filing date of record is deemed to be 4/16/2004.

Response to Arguments

It is noted that the priority to the prior filed applications was denied in the previous office actions (1/08/2009 and 4/18/2009). The reply did not traverse the denial of priority to the prior filed applications. As such, the denial of priority to the prior filed applications is being maintained.

Information Disclosure Statement

10. The information disclosure statement (IDS) submitted on 10/08/09 has been considered by the examiner. The reference of "APO Office Action, Australian Patent

Application No. 2004233009, September 15, 2009" was cross through as the cited reference fails to meet all the requirements set forth in MPEP 609 as the office action does not have an actual publication date. However, the reference has nevertheless been considered by the examiner. A copy of the IDS with the examiners initials and date has been provided along with this office action.

The IDS submitted on 5/31/2005 was previously considered by the examiner. However, upon review of 5/31/2005, references (CN1450172A; WO04/057021A2; Drosten et al. NEM April 10, 2003; Grondahl et al. J. Clin. Microbiol. 1999; Kehl et al. J. Clin. Microbiol. 2001; Lau et al. Biophys Res Comm 2003; Vabret et al. J. Virol Meth 2001; and Zhou et al. Virologica Siniga 2003) have been initialed but cross-through as these references are duplicates of the IDS submitted on 12/20/2004.

Lai, "Coronavirus leader RNA primed transcription an alternative mechanism in RNA splicing" BioEssays 5(6) p. 257-260, has been corrected by the examiner to include the date of publication.

Further the reference, "Artus SARS Test" Abbott Laboratories" has been cross through but considered as the cited reference fails to meet all the requirements set forth in MPEP 609 as the office action does not have an actual publication date. A copy of the IDS of 5/31/2005 has also been provided along with this office action.

It is noted for clarity in the record, that the IDS submitted on 9/12/2005 and 12/20/2004 have previously been considered by the examiner and therefore these IDS are not provided with the instant office action.

Drawings

11. The drawings submitted on 4/16/2004 are objected to because the lines on the graph of Figure 1 can not be distinguished from one another. Specifically the legend indicates that each line of the figure represents a specific copy number; however, the individual line types can not be discerned in the figure. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

12. Claims 116 and 125-130 objected to because of the following informalities: Claim 116 recites “HCoV-OC43 or HCoV-229E”. Abbreviations should be spelled out in independent claims for clarity. It is suggested that the applicant amend the claims to e.g. “human coronavirus OC43 (HCoV-043) or human coronavirus 229E (HCoV-229E)”. Appropriate correction is required.

Claim Rejections - 35 USC § 112/2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 116 and 125-130 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 116 and 125-130 are indefinite. Claim 116 recites the limitation "said target sequence" in 7-8. There is insufficient antecedent basis for this limitation in the claim. Specifically, it is not clear if the target sequence is referring to the SCARS-CoV in the test sample or some other undefined target sequence. It is suggested to correct this antecedent basis the claim be amended to e.g. "a target sequence".

Claim 125 recites the limitation "the base sequence of said probe" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. There is insufficient antecedent basis because it is unclear if "the base sequence" is referring to the base sequence of the target binding portion as recited in Claim 116 or some other undefined

base sequence. It is suggested that the claim be amended to correct the antecedent basis by amending the claim to e.g. "a base sequence of said probe consist of the base sequence of SEQ ID NO. 7".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 116 and 127-130 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drosten et al. (New England Journal of Medicine Published online April 10, 2003 Vol. 348 p. 1967-1976) in view of Hogan (US Patent 5541308 July 30, 1996) and McDonough et al. (WO 94/23069 October 13, 1994).

See IDS filed 12/20/2004 for Drosten et al. reference.

Claim 116 is interpreted as a detection probe which comprises a target binding portion consisting of SEQ ID NO. 4. Claim 116 requires that the probe does not comprise any other base sequences which stably hybridize to nucleic acid derived from SARS-CoV under stringent hybridization conditions and does not form a hybrid stable for detection with nucleic acid derived form HCoV-OC43 or HC0V-229E. This claim language is being interpreted as the detection probe comprises no nucleotides flanking SEQ ID No. 4 which are identical to nucleotides which represent the nucleic acid structure of SARS-CoV. Therefore although the detection probe has comprising language, it consists of only the nucleotides of SEQ ID NO. 4 with respect to the nucleotide structure of SARS-CoV. The language "derived from" is being interpreted as nucleic acids which represent the nucleotide structure of SARS-CoV, HCoV-OC43 or HCoV-229E

With regard to Claim 116, Drosten et al. teaches a probe sequence BNITMSARP (Table 1). This sequence encompasses SEQ ID No. 4 of the instant specification. Specifically SEQ ID No. 4 is 100% identical to nucleotides 2-19 of the 24 mer BNITMSARP. Drosten et al. teaches that this probe was used in a PCR assay and that it did not cross react with human coronaviruses 229E and OC43 and as such would not form a stable hybrid with these coronaviruses under stringent hybridization conditions (p. 1971 last paragraph through 1972 1st paragraph).

Drosten et al. further provides an alignment of the isolated region of the SARs virus which includes the sequence represented by BNITMSARP (Figure 1B). The

BNITMSARP sequence is located at positions 99-122 of the BN1-1 sequence of Figure 1B and therefore SEQ ID No. 4 is located at positions 100-117 of the BN1-1 sequence of Figure 1B. Drosten et al. teaches that the isolated 300 nucleotide fragment (e.g. BN1-1) of the SARS nucleotide structure is only distantly related to known coronaviruses (50 to 60%) (abstract). Therefore Drosten et al. teaches that detection in this fragment using conventional and real time PCR assay can specifically and sensitively detect the SARs virus (abstract). As such Drosten et al. provides a region of the SARs virus (300 bp in length) which is distinct from the known coronaviruses of 229E and OC43 and therefore fragments of nucleic acids in this region would specifically detect a target sequence of a SARs-CoV and not specifically detect the known coronaviruses of 229E and OC43. Therefore, although Drosten et al. does not teach a detection probe comprising a target binding portion consisting of SEQ ID No. 4 and no other nucleotides which hybridize to the SARs-CoV, Drosten et al. does provide a 300 bp region of the SARs-CoV. Drosten et al. further states that this region is only distantly related to 229E and OC43, provides an alignment, and teaches that probes in this region can specifically detect SARs-CoV in a sample.

With regard to Claims 127 and 128, Drosten et al. teaches that probes are labeled with carboxyfluorescein on the 3' end and tetramethylrhodamin on the 5' end (e.g. a luminescent and quencher pair) (Table 1).

With regard to Claim 129, Drosten et al. teaches that the probe label fluorescence is measured (Table 1 including the legend indicating that fluorescence was measured).

With regard to Claim 130, this claim is drawn to use statements regarding the hybridization stringency of binding the claimed probe to a target. The phrase "conditions include a temperature of about 60°C and a salt concentration of about 0.6M to about 0.9M" does not limit the claimed probe to a particular structure, but rather requires that the probe to be able to hybridize to a target under particular hybridization conditions. Any probe which encompasses the structure claimed would be capable of hybridization to a target under the claimed conditions. As such the recitation of the use language in the claim does not provide a structural limitation to the claimed detection probe over the prior art.

However, Drosten et al. does not teach that the probe sequence has a target binding region consisting of SEQ ID NO. 4 and that the probe does not comprise any other base sequences which stably hybridize to nucleic acid derived from SARS-CoV.

However, it was well known in the art at the time of filing that the ordinary artisan can make any number of probes to a known region with the predictable use of detecting a particular target sequence.

With regard to claim 116, Hogan teaches the use of specific probes to amplify a particular region of bacteria. Hogan et al. provides guidance for the selection of probes.

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> Fist, probes should be positioned so as to minimize the stability of the probe: nontarget nucleic acid hybrid. This may be accomplished by minimizing the

> length of perfect complementarily to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe: target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G: C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10 ºC higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structure inhibitory to hybridization are less preferred. Finally probes with extensive self complementarity should be avoided." (See Column 6 lines 66-67 and Column 7 lines 1-29).

Hogan teaches that "while oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 15 and about 50 bases in length" (see Column 10, lines 13-15). SEQ ID No. 4 would be encompassed by this teaching of length as SEQ ID No. 4 is 17 bases in length.

Therefore Hogan et al. teaches design optimization to make any number of probes to a given region. Although Hogan et al. does not specifically teach design of probes using virus targets, but rather "non-virus" targets, the art at the time of filing taught that the ordinary artisan could use the design optimization techniques taught by Hogan to design probes directed towards a viral target.

McDonough teaches methods of detecting HIV (e.g. a viral sample) by use of oligonucleotides (abstract). McDonough teaches, "Useful guidelines for designing amplification oligonucleotides and probes with desired characteristics are described herein. The optimal sites for amplifying and probing contain two, and preferably three, conserved regions greater than about 15 bases in length, within about 350 bases, and

preferably within 150 bases, of contiguous sequence. The degree of amplification observed with a set of primers or promoter/primers depends on several factors, including the ability of the oligonucleotides to hybridize to their complementary sequences and their ability to be extended enzymatically. Because the extent and specificity of hybridization reactions are affected by a number of factors, manipulation of those factors will determine the exact sensitivity and specificity of a particular oligonucleotide, whether perfectly complementary to its target or not. The importance and effect of various assay conditions are known to those skilled in the art as described by Hogan et al, EPO Patent Application NO. PCT/US87/03009, entitled "Nucleic Acid Probes for Detection and/or Quantitation of Non-Viral Organisms." Hogan (US Patent 5541308, issued July 30, 1996) is a continuation of PCT/US87/03009. As such, McDonough teaches that routine optimization and design of probes from viral targets can be done by using the optimization constraints of Hogan. Therefore the teachings of the art suggest that probes toward viral targets, such as SARs Co-V, can be designed and optimized using the teaching of Hogan.

Since the claimed probe represents structural homologs, which are derived from sequences suggested by the prior art as useful for probes for the detection of SARS-CoV, and considering that a person of ordinary skill in the art would attempt to obtain alternate compounds with improved properties, the claimed probes are prima facie obvious over the cited references in the absence of secondary considerations. Therefore, it would have been prima facie obvious to produce any number of fragments and design probes from the Bn1-1 region taught by Drosten et al., including probes

consisting of SEQ ID No. 4, using the design constraints taught by Hogan and McDonough et al. The art of designing probes and primers at the time the invention was made was very well described in the art. Designing probes and primers that are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan et al. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes and primers to detect. The ordinary artisan would be motivated therefore to design any number of probes from the region taught by Drosten et al including probes consisting of SEQ ID No. 4 with the reasonable expectation that any fragment from the Bn1-1 region taught by Drosten et al. would be able to detect the SARS-CoV in a test sample and not hybridize to HCoV-OC43 or HCoV-229E. From the teachings and suggestions of the cited references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidence by the references, especially in the absence of evidence to the contrary. The artisan would have a reasonable expectation of success as the artisan is merely substituting one SARs Co-V genome fragment for another in a specific region which has already been analyzed for its ability to specifically detect the SARs virus in a sample (e.g. the 300 bp BN1-1 region taught by Drosten et al.) using design constraints known in the art at the time of filing (Hogan and McDonough et al). The ordinary artisan would be motivated

to have designed and test new probes to obtain additional oligonucleotides that function to detect SARs Co-V and identify oligonucleotides with improved properties.

16. Claims 125-126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drosten et al. (New England Journal of Medicine Published online April 10, 2003 Vol. 348 p. 1967-1976), Hogan (US Patent 5541308 July 30, 1996), and McDonough et al. (WO 94/23069 October 13, 1994) as applied to claims 116 and 127-130 and in view of Tyagi et al. (US Patent 5925517 July 1999).

The combination of Drosten et al, Hogan, and McDonough et al. suggest a detection probe comprising a target binding portion consisting of SEQ ID No. 4, however, this combination does not teach SEQ ID NO. 7 or that the probe is self hybridizing. The claim is being interpreted for art purposes as being drawn to a detection probe comprising SEQ ID No. 7.

SEQ ID No. 7 encompasses the RNA equivalent of SEQ ID No. 4 (see underlined portion) and has artificial nucleotides added to allow the probe to form a molecular beacon probe (see bolded section which indicates the self hybridizing portion).

SEQ ID NO. 7 **C<u>CGUG</u>**CGUGGAUUGGCUUU**<u>CACGG</u>**

Although the art does not teach this specific SEQ ID Number, the art suggests methodologies to design hairpin probes from known sequences. Further, the design of

such a probe would be routine optimization based upon the known detection sequence provided by Drosten et al.

With regard to Claim 125, Tyagi et al. provides guidance for the routine design of molecular beacon probes (e.g. self hybridizing probes). Tyagi et al. teaches that use of these types of probes allows for the increased discrimination between hybridization of the probe to the target and unhybridized probes, as unhybridized probes will show little or no signal generation (Column 3 lines 30-45 and 55-60). As such the art teaches motivation to design molecular beacon probes to detect targets in a sample.

Tyagi et al. teaches that the probes are designed so that the there is a single stranded nucleic acid region that is complementary to a desired target nucleic acid and 5' and 3' regions flanking this target region that reversibly interact (column 4 lines 60-66). As such Tyagi et al. teaches the design of probes that are self hybridizing when the target is not present in the sample.

Tyagi et al. teaches that the probes can be made from DNA or RNA (column 8 lines 66-67). Therefore depending on the hybridization assay used by the ordinary artisan, targets in samples can be detected using probes comprising DNA or RNA structures designed by the optimization conditions of Tyagi et al. Herein in the instant case, the RNA and DNA structures are equivalent structures of the group of nucleic acids. These equivalent structures are used by the ordinary artisan in different hybridization assays; however, both RNA and DNA structure in the claimed region would equivalently detect the same target region of the SARs Co-V and therefore are structural equivalents.

Tyagi et al. teaches that to construct the probes the stems (e.g. the arms which hybridize to each other when the target is not present) and the lengths of target complement sequences are chosen for the proper thermodynamic functioning of the probe under the conditions of the projected hybridization assay (Column 11 lines 22-25). Tyagi et al. teaches that persons skilled in hybridization assays will understand that pertinent conditions including probe, target and solute concentrations, detection temperature, presence of denaturants and volume excluders, and other hybridization inducing factors (column 11 lines 25-30) can be routinely optimized. Tyagi et al. teaches that length of the target complement sequence can range form 7 to 140 nucleotides, preferably from 10 to 140 nucleotides (column 11 lines 30-35 and column 12 lines 35-45). Tyagi et al. teaches that arm sequences should be of sufficient length that under conditions of the assay and at the detection temperature, when the probe is not bound to a target, the arms are associated and the labeling moieties at the 5' and 3' ends are in close proximity to each other (column 12 lines 53-55). Tyagi et al. teaches depending on the assay conditions used, 3 to 25 nucleotide arm lengths can be used (column 12 lines 55-58). Tyagi et al. teaches that the actual length will be chosen with reference to the target complement sequence such that the probe remains in closed conformation in the absence of the target and assumes an open conformation when bound to the target (column 12 lines 57-60). Herein in the instant case, the region which can specifically detect SARs Co-V in a sample has been taught by Drosten et al. Tyagi et al teaches that the design of a molecular beacon type probe from this known region is routine optimization of the hybridization conditions used in the assay

performed by the ordinary artisan. Herein in the instant case, the length of the target complement sequence encompassed by SEQ ID No. 7 and the arm length of SEQ ID No. 7 falls within the parameters taught by Tyagi et al.

Tyagi et al. teaches that the upper length of the arm is governed by the melting temperature of the arm stem which should be higher than the detection temperature of the assay and the energy released by the formation of the stem should be less than the energy released by the formation of the target complement sequence target sequence (e.g. the arm sequence should be shorter than the target complement) (column 13 lines 1-15). Herein in the instant case the arm length of SEQ ID No. 7 is 5 nucleotides which is less than the length of the target complement sequence encompassed by SEQ ID No. 7. Therefore SEQ ID No. 7 encompasses the routine optimization constraints taught by Tyagi et al.

Tyagi et al. teaches that the probe can be designed within parameters which allows the probe to shift to open conformation only when the target sequences is a perfect complement to the target complement region of the sequence (Column 14 lines 10-15). Tyagi et al. teaches that target complement sequences should be from 7 to 25 nucleotides with arm sequences from 3 to 8 nucleotides (column 14 lines 10-15). Tyagi et al. teaches that the guanosine-cytidine content of the stem duplex, the probe target hybrid, salt and assay temperature should all be considered (column 14 lines 9-15). Further, Tyagi et al. teaches that complementary sequences may be placed within an arm adjacent to the target complement sequence (column 16 lines 1-5). Tyagi et al. teaches that one arm sequence may be completely or partially complementary to the

target to increase the thermodynamic stability of the open confirmation (column 16 lines 1-10). Herein SEQ ID No. 7 comprises an arm which is 5 nucleotides in length and encompasses complementary sequences to the target. As such the design of SEQ ID No. 7 is encompassed by the optimization and design strategies of Tyagi et al.

Tyagi et al. teaches that the probe is constructed depending up the hybridization conditions and as such the length and nucleotides contained in the stem duplex will change depending on the assay conditions used (column 14 lines 45-60). Therefore Tyagi et al. teaches that it is routine optimization to design molecular beacons to specifically detect targets. Herein in the instant case, Drosten et al. teaches a region of 300 bp in the SARs Co-V nucleotide structure which can specifically and sensitively detect SARs in a sample. The design of artificial nucleotides around probes designed from this region in order to produce a molecular beacon would be routine optimization by the ordinary artisan.

With regard to Claim 126, Tyagi et al. teaches that the probes are designed so that the there is a single stranded nucleic acid region that is complementary to a desired target nucleic acid and 5' and 3' regions flanking this target region that reversibly interact (column 4 lines 60-66). Therefore Tyagi et al teaches that the probe is self hybridizing when the target is not present.

Therefore the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidence by the references, especially in the absence of evidence to the contrary. The teaching of Drosten et al, Hogan, and McDonough teach the design of probes to a region of the SARs genome

which will specifically detect the SARs virus in a sample and does not hybridize to HCoV-OC43 or HCoV229E. Therefore the combination teaches probes which are specific and sensitive to SARs Co-V. Although, the prior art does not teach the explicit structure of SEQ ID No. 7, the art (Tyagi et al.) does teach the design and optimization of molecular beacons to detect targets in a sample.

SEQ ID No. 7 encompasses the RNA equivalent to SEQ ID No. 4. Tyagi et al. teaches that molecular beacons can be constructed which encompass target binding regions of either RNA or DNA structure (column 8 lines 66-67). An obviousness determination is not the result of a rigid formula disassociated form the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."). Herein in the instant case, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use either the DNA or RNA structure of SEQ ID NO. 4 to detect the SARS virus in a sample depending of the hybridization assay used. RNA and DNA are structural homologs in which each one would identically detect the same target region in a sample. As such it would have been obvious to one of ordinary skill in the art and the ordinary artisan would have had a reasonable expectation of success to substitute one nucleic acid structure for another to detect the SARS virus in a sample.

Further it would have been obvious, absent secondary considerations, to design probes

from the region taught by Drosten et al. which are self hybridizing. Tyagi et al. teaches that use of these types of probes allows for the increased discrimination between hybridization of the probe to the target and unhybridized probes, as unhybridized probes will show little or no signal generation (Column 3 lines 30-45 and 55-60). As such the art teaches motivation to design molecular beacon probes to detect targets in a sample. Tyagi et al. teaches that the design of such probes from known regions (e.g. the BN1-1 region taught by Drosten et al.) is routine for the ordinary artisan. As shown in the rejection above, the structure of SEQ ID No. 7 is encompassed by the design and optimization conditions provided by Tyagi et al. It would therefore be obvious to one of ordinary skill in the art, absent secondary considerations, to design any number of molecular beacon probes encompassing the target complementary region taught by Drosten et al., Hogan, and McDonough et al. using the optimization parameters of Tyagi et al. with a reasonable expectation of success of producing a self hybridizing probe which detects SARs Co-v. As shown in the teachings of Tyagi et al. the design of molecular beacons (self hybridizing probes) encompassing a known target complementary region is routine optimization. Therefore the ordinary artisan would be motivated to design any number of molecular beacon probes which encompass the target complementary region of Drosten et al., Hogan, and McDonough et al. using the optimization constraints of Tyagi et al. including the specific probe comprising SEQ ID No. 7. The ordinary artisan would be motivated to have designed and test new self hybridizing probes to obtain additional oligonucleotides that function to detect SARs Co-V and identify oligonucleotides with improved properties.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday - Friday 9AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Katherine Salmon/
Examiner, Art Unit 1634